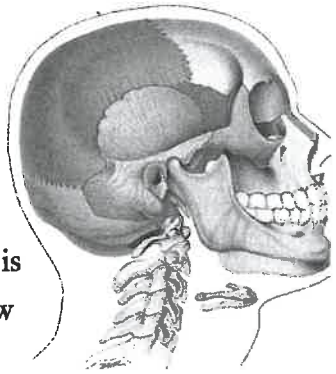
THE SKELETAL SYSTEM

chapter 6

Introduction



did you know?

People are encouraged to limit food intake and exercise regularly to prevent obesity and stay healthy. But people who go to extremes can compromise the health of their bones. Premature osteoporosis can occur in young women who experience prolonged menstrual irregularity, which is often caused by extreme dieting and/or excessive exercise. These women have low levels of the estrogens, hormones which help to keep bones strong. Extreme dieting behavior may mean a minimal calcium intake, which then limits the body's bone-building ability. People who build strong bones during adolescence and young adulthood reduce their likelihood of developing osteoporosis later in life.

Focus on Wellness, page 148

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Despite its simple appearance, bone is a complex and dynamic living tissue that is remodeled continuously—new bone is built while old bone is broken down. Each individual bone is an organ composed of several different tissues working together: bone, cartilage, dense connective tissues, epithelium, blood-forming tissue, adipose tissue, and nervous tissue. The entire framework of bones and their cartilages constitute the ***skeletal system***. The study of bone structure and the treatment of bone disorders is termed ***osteology*** (os′-tē-OL-ō-jē; *osteo-* = bone; *-logy* = study of).

looking back to move ahead . . .

- **Connective Tissue Extracellular Matrix (page 83)**
- **Cartilage (page 89)**
- **Bone Tissue (page 89)**
- **Collagen Fibers (page 84)**
- **Dense Irregular Connective Tissue (page 87)**

FUNCTIONS OF BONE AND THE SKELETAL SYSTEM

OBJECTIVE • Discuss the functions of bone and the skeletal system.

Bone tissue and the skeletal system perform several basic functions:

1. **Support.** The skeleton provides a structural framework for the body by supporting soft tissues and providing points of attachment for most skeletal muscles.
2. **Protection.** The skeleton protects many internal organs from injury. For example, cranial bones protect the brain, vertebrae (backbones) protect the spinal cord, and the rib cage protects the heart and lungs.
3. **Assisting in movement.** Because most skeletal muscles attach to bones, when muscles contract, they pull on bones. Together bones and muscles produce movement. This function is discussed in detail in Chapter 8.
4. **Mineral homeostasis.** Bone tissue stores several minerals, especially calcium and phosphorus. On demand, bone releases minerals into the blood to maintain critical mineral balances (homeostasis) and to distribute the minerals to other parts of the body.
5. **Production of blood cells.** Within certain bones a connective tissue called ***red bone marrow*** produces red blood cells, white blood cells, and platelets, a process called ***hemopoiesis*** (hēm-ō-poy-Ē-sis; *hemo-* = blood; *poiesis* = making). Red bone marrow consists of developing blood cells, adipocytes, fibroblasts, and macrophages. It is present in developing bones of the fetus and in some adult bones, such as the pelvis, ribs, sternum (breastbone), vertebrae (backbones), skull, and ends of the arm bones and thigh bones.
6. **Triglyceride storage.** ***Yellow bone marrow*** consists mainly of adipose cells, which store triglycerides. The stored triglycerides are a potential chemical energy reserve. Yellow bone marrow also contains a few blood cells. In the newborn, all bone marrow is red and is involved in hemopoiesis. With increasing age, much of the bone marrow changes from red to yellow.

■ CHECKPOINT

1. What kinds of tissues make up the skeletal system?
2. How do red and yellow bone marrow differ in composition, location, and function?

TYPES OF BONES

OBJECTIVE • Classify bones on the basis of their shape and location.

Almost all the bones of the body may be classified into four main types based on their shape: long, short, flat, or irregular. ***Long bones*** have greater length than width and consist of a shaft and a variable number of ends. They are usually somewhat curved for strength. Long bones include those in the thigh (femur), leg (tibia and fibula), arm (humerus), forearm (ulna and radius), and fingers and toes (phalanges).

Short bones are somewhat cube-shaped and nearly equal in length and width. Examples of short bones include most wrist and ankle bones.

Flat bones are generally thin, afford considerable protection, and provide extensive surfaces for muscle attachment. Bones classified as flat bones include the cranial bones, which protect the brain; the sternum (breastbone) and ribs, which protect organs in the thorax; and the scapulae (shoulder blades).

Irregular bones have complex shapes and cannot be grouped into any of the previous categories. Such bones include the vertebrae and some facial bones.

■ CHECKPOINT

3. Give several examples of long, short, flat, and irregular bones.

STRUCTURE OF BONE

OBJECTIVES • Describe the parts of a long bone.
• Describe the histological features of bone tissue.

We will now explore the structure of bone at both the macroscopic and microscopic levels.

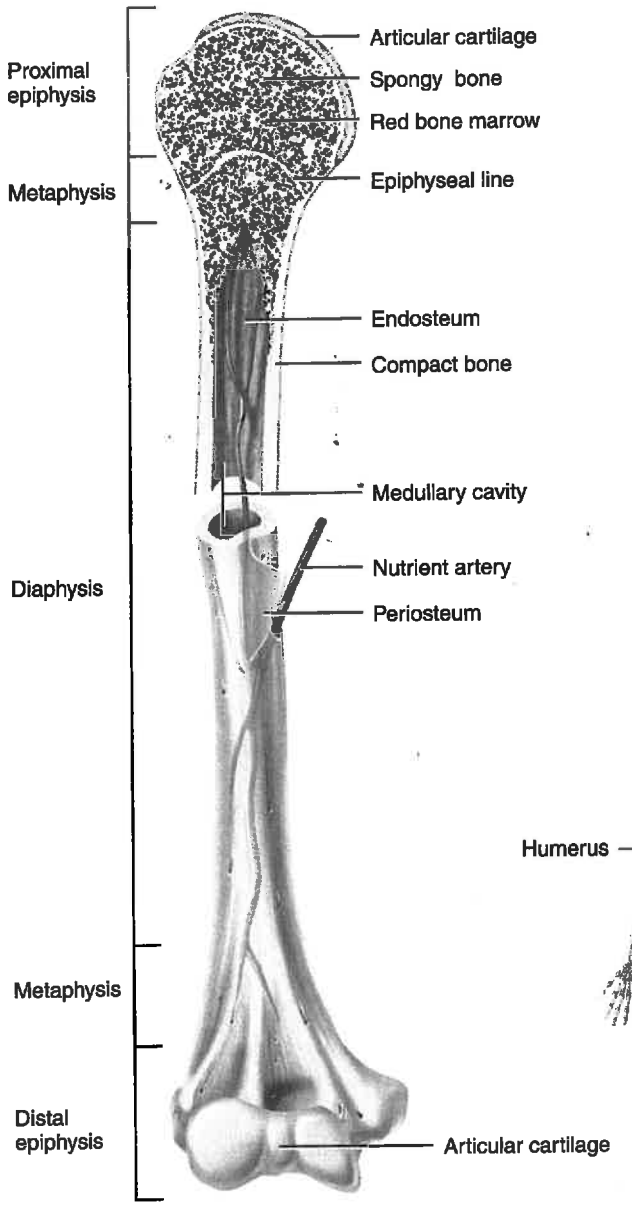
Macroscopic Structure of Bone

The structure of a bone may be analyzed by considering the parts of a long bone, for instance, the humerus (the arm bone), as shown in Figure 6.1. A typical long bone consists of the following parts:

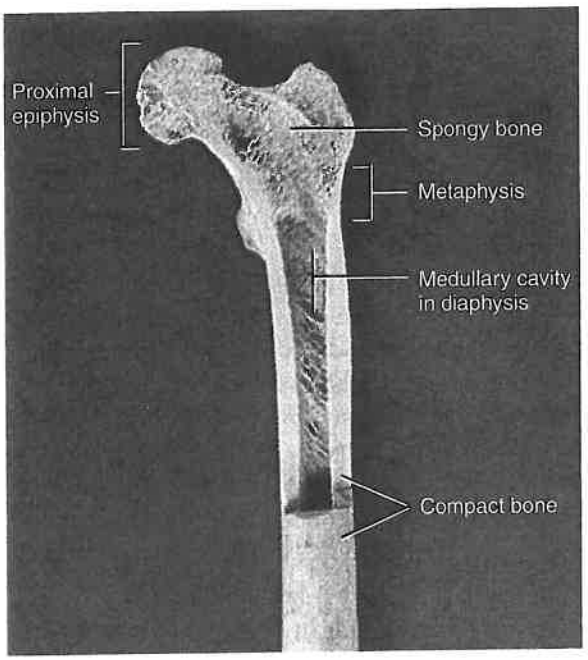
1. The ***diaphysis*** (dī-AF-i-sis = growing between) is the bone's shaft or body—the long, cylindrical, main portion of the bone.
2. The ***epiphyses*** (e-PIF-i-sēz = growing over; singular is *epiphysis*) are the distal and proximal ends of the bone.

Figure 6.1 Parts of a long bone: epiphysis, metaphysis, and diaphysis. The spongy bone of the epiphysis and metaphysis contains red bone marrow, and the medullary cavity of the diaphysis contains yellow bone marrow in an adult.

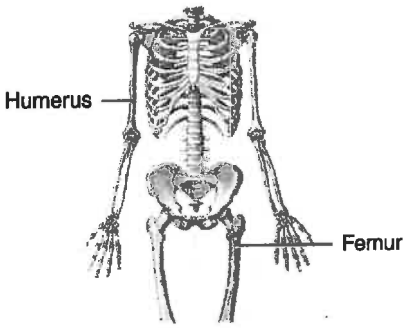
A long bone is covered by articular cartilage at its proximal and distal epiphyses and by periosteum around the remainder of the bone.



(a) Partially sectioned humerus (arm bone)



(b) Partially sectioned femur (thigh bone)



Functions of Bone Tissue

1. Supports soft tissues and provides attachment for skeletal muscles.
2. Protects internal organs.
3. Assists in movement together with skeletal muscles.
4. Stores and releases minerals.
5. Contains red bone marrow, which produces blood cells.
6. Contains yellow bone marrow, which stores triglycerides (fats), a potential chemical energy source.

Which part of a bone reduces friction at joints? Produces blood cells? Lines the medullary cavity?

3. The ***metaphyses*** (me-TAF-i-sēz; *meta-* = between; singular is *metaphysis*) are the regions in a *mature bone* where the diaphysis joins the epiphyses. In a *growing bone*, each metaphysis contains an *epiphyseal plate* (ep′-i-FIZ-ē-al), a layer of hyaline cartilage that allows the diaphysis of the bone to grow in length (described later in the chapter). When bone growth in length stops, the cartilage in the epiphyseal plate is replaced by bone and the resulting bony structure is known as the *epiphyseal line*.
4. The ***articular cartilage*** is a thin layer of hyaline cartilage covering the part of the epiphysis where the bone forms an articulation (joint) with another bone. Articular cartilage reduces friction and absorbs shock at freely movable joints. Because articular cartilage lacks a perichondrium, repair of damage is limited.
5. The ***periosteum*** (per′-ē-OS-tē-um; *peri-* = around) is a tough sheath of dense irregular connective tissue that surrounds the bone surface wherever it is not covered by articular cartilage. The periosteum contains bone-forming cells that enable bone to grow in diameter or thickness, but not in length. It also protects the bone, assists in fracture repair, helps nourish bone tissue, and serves as an attachment point for ligaments and tendons.
6. The ***medullary cavity*** (MED-ū-lar′-ē; *medulla-* = marrow, pith) or *marrow cavity* is a hollow, cylindrical space within the diaphysis that contains fatty yellow bone marrow in adults.
7. The ***endosteum*** (end-OS-tē-um; *endo-* = within) is a thin membrane that lines the medullary cavity. It contains a single layer of bone-forming cells.

Microscopic Structure of Bone

Like other connective tissues, ***bone***, or ***osseous tissue*** (OS-ē-us) contains abundant extracellular matrix that surrounds widely separated cells. The extracellular matrix is about 25% water, 25% collagen fibers, and 50% crystallized mineral salts. As these mineral salts are deposited in the framework formed by the collagen fibers of the extracellular matrix, they crystallize and the tissue hardens. This process of ***calcification*** is initiated by osteoblasts, the bone-building cells.

Although a bone's *hardness* depends on the crystallized inorganic mineral salts, a bone's *flexibility* depends on its collagen fibers. Like reinforcing metal rods in concrete, collagen fibers and other organic molecules provide *tensile strength*, which is resistance to being stretched or torn apart.

Four major types of cells are present in bone tissue: osteogenic cells, osteoblasts, osteocytes, and osteoclasts (Figure 6.2a).

1. ***Osteogenic cells*** (os-tē-ō-JEN-ik; *-genic* = producing) are unspecialized stem cells derived from mesenchyme, the tissue from which all connective tissues are formed. They are the only bone cells to undergo cell division; the resulting cells develop into osteoblasts. Osteogenic cells are found along the inner portion of the periosteum, in the endosteum, and in the canals within bone that contain blood vessels.
2. ***Osteoblasts*** (OS-tē-ō-blasts′; *-blasts* = buds or sprouts) are bone-building cells. They synthesize and secrete collagen fibers and other organic components needed to build the extracellular matrix of bone tissue. As osteoblasts surround themselves with matrix, they become trapped in their secretions and become osteocytes. (Note: *Blasts* in bone or any other connective tissue secrete matrix.)
3. ***Osteocytes*** (OS-tē-ō-sīts′; *-cytes* = cells), mature bone cells, are the main cells in bone tissue and maintain its daily metabolism, such as the exchange of nutrients and wastes with the blood. Like osteoblasts, osteocytes do not undergo cell division. (Note: *Cytes* in bone or any other tissue maintain the tissue.)
4. ***Osteoclasts*** (OS-tē-ō-clasts′; *-clast* = break) are huge cells derived from the fusion of as many as 50 monocytes (a type of white blood cell) and are concentrated in the endosteum. They release powerful lysosomal enzymes and acids that digest the protein and mineral components of the bone extracellular matrix. This breakdown of bone extracellular matrix, termed *resorption*, is part of the normal development, growth, maintenance, and repair of bone. (Note: *Clasts* in bone break down extracellular matrix.)

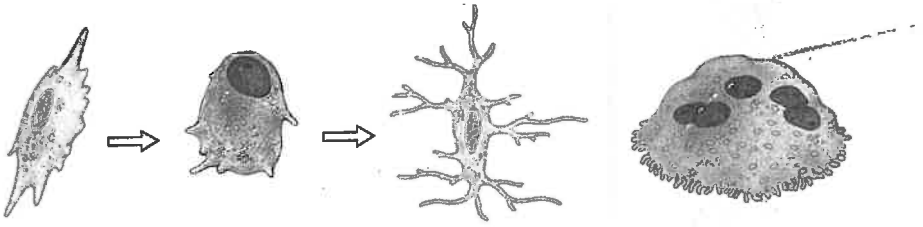
Bone is not completely solid but has many small spaces between its cells and extracellular matrix components. Some spaces are channels for blood vessels that supply bone cells with nutrients. Other spaces are storage areas for red bone marrow. Depending on the size and distribution of the spaces, the regions of a bone may be categorized as compact or spongy (see Figure 6.1). Overall, about 80% of the skeleton is compact bone and 20% is spongy bone.

Compact Bone Tissue

Compact bone tissue contains few spaces and is arranged in repeating units called ***osteons*** or ***haversian systems*** (Figure 6.2c). Each osteon consists of a central (haversian) canal with its concentrically arranged lamellae, lacunae, osteocytes, and canaliculi. A ***central*** or ***haversian*** (ha-VER-shun) ***canal*** is a channel that contains blood vessels, nerves, and lymphatic vessels. The central canals run longitudinally through the bone. Around the canals are ***concentric lamellae*** (la-MEL-ē)—rings of hard, calcified extracellular matrix. Between the lamellae are small spaces called ***lacunae*** (la-KOO-nē = little lakes; singular is *lacuna*), which contain osteocytes. Radiating in all directions from the lacunae are tiny ***canaliculi*** (kan′-a-LIK-ū-lī = small channels), which are filled with extracellular fluid. Inside the canaliculi are slender fingerlike processes of osteocytes (see inset at right of Figure 6.2c). The canaliculi connect lacunae with one another and with the central canals. Thus, an intricate, miniature canal system throughout the bone provides many routes for nutrients and oxygen to reach the osteocytes and for wastes to diffuse away. This is very important because diffusion through the lamellae is extremely slow.

Figure 6.2 Histology of bone.

Osteocytes lie in lacunae arranged in concentric circles around a central (haversian) canal in compact bone, and in lacunae arranged irregularly in the trabeculae of spongy bone.



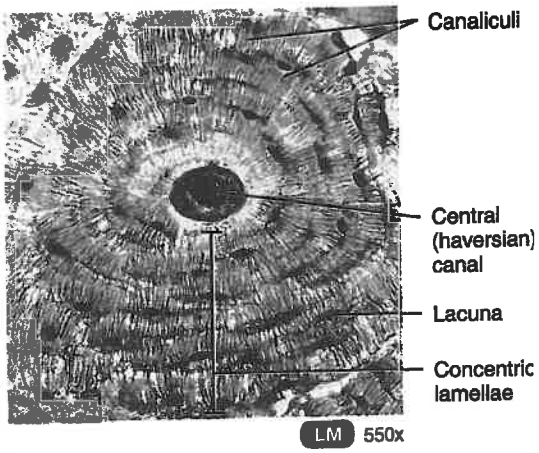
Osteogenic cell (develops into an osteoblast)

Osteoblast (forms bone extracellular matrix)

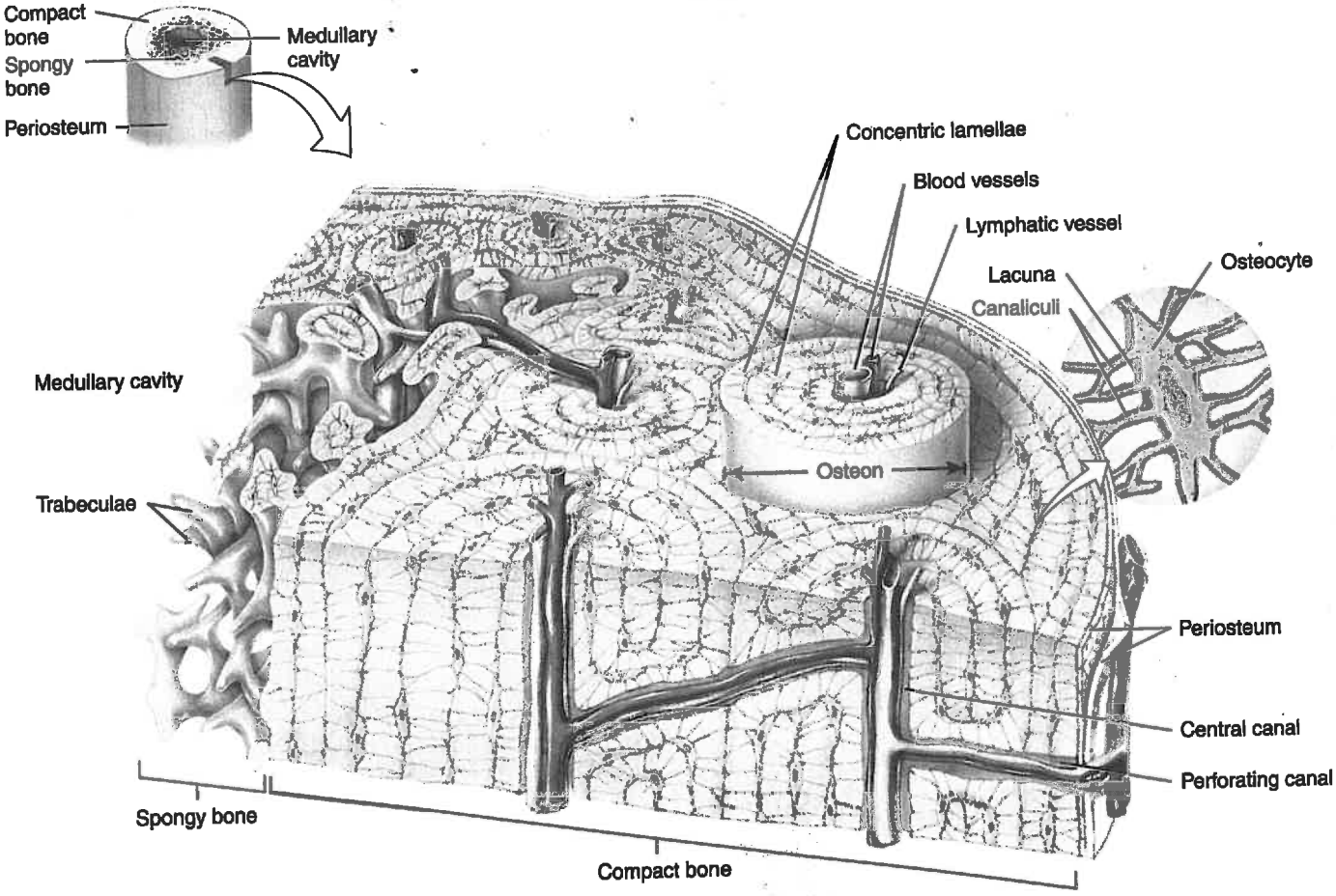
Osteocyte (maintains bone tissue)

Osteoclast (functions in resorption, the breakdown of bone matrix)

(a) Types of cells in bone tissue



(b) Sectional view of an osteon (haversian system)



(c) Osteons (haversian systems) in compact bone and trabeculae in spongy bone

As people age, some central (haversian) canals may become blocked. What effect would this have on the osteocytes?

Blood vessels, lymphatic vessels, and nerves from the periosteum penetrate the compact bone through transverse ***perforating (volkmann's) canals***. The vessels and nerves of the perforating canals connect with those of the medullary cavity, periosteum, and central (haversian) canals.

Compact bone tissue contains few spaces. It is found beneath the periosteum of all bones and makes up the bulk of the diaphyses of long bones. Compact bone tissue provides protection and support and resists the stresses produced by weight and movement.

Spongy Bone Tissue

In contrast to compact bone tissue, ***spongy bone tissue*** does not contain osteons. As shown in Figure 6.2c it consists of units called ***trabeculae*** (tra-BEK-ū-lē = little beams; singular is *trabecula*), an irregular latticework of thin columns of bone. The macroscopic spaces between the trabeculae of some bones are filled with red bone marrow. Within each trabecula are osteocytes that lie in lacunae. Radiating from the lacunae are canaliculi.

Spongy bone tissue makes up most of the bone tissue of short, flat, and irregularly shaped bones. It also forms most of the epiphyses of long bones and a narrow rim around the medullary cavity of the diaphysis of long bones.

Spongy bone tissue is different from compact bone tissue in two respects. First, spongy bone tissue is light, which reduces the overall weight of a bone so that it moves more readily when pulled by a skeletal muscle. Second, the trabeculae of spongy bone tissue support and protect the red bone marrow. The spongy bone tissue in the hip bones, ribs, breastbone, backbones, and the ends of long bones is the only site where red bone marrow is found and, thus, the site of blood cell production in adults.

In a **bone scan**, a small amount of a radioactive tracer compound that is readily absorbed by bone is injected intravenously. The degree of uptake of the tracer is related to the amount of blood flow to the bone. Normal bone tissue is identified by a consistent gray color throughout because of its uniform uptake of the radioactive tracer. Darker or lighter areas may indicate bone abnormalities. Darker areas called "hot spots" are areas of increased metabolism that absorb more of the radioactive tracer due to increased blood flow. Hot spots may indicate bone cancer, abnormal healing of fractures, or abnormal bone growth. Lighter areas called "cold spots" are areas of decreased metabolism that absorb less of the radioactive tracer due to decreased blood flow. Cold spots may indicate problems such as degenerative bone disease, decalcified bone, fractures, bone infections, Paget's disease, or rheumatoid arthritis. A bone scan detects abnormalities 3 to 6 months sooner than standard x-ray procedures and exposes the patient to less radiation. A bone scan is the standard test for bone density screening, particularly for osteoporosis in females.

■ **CHECKPOINT**

4. Diagram the parts of a long bone, and list the functions of each part.
5. What are the four types of cells in bone tissue?
6. How are spongy and compact bone tissue different in terms of their microscopic appearance, location, and function?

BONE FORMATION

OBJECTIVES • **Explain the importance of bone formation during different phases of a person's lifetime.**

• **Describe the factors that affect bone growth during a person's lifetime.**

The process by which bone forms is called ***ossification*** (os'-i-fi-KĀ-shun; *ossi-* = bone; *-fication* = making). Bone formation occurs in four principal situations: (1) the initial formation of bones in an embryo and fetus, (2) the growth of bones during infancy, childhood, and adolescence until their adult sizes are reached, (3) the remodeling of bone (replacement of old bone tissue by new bone tissue throughout life); and (4) the repair of fractures (breaks in bones) throughout life.

Initial Bone Formation in an Embryo and Fetus

We will first consider the initial formation of bone in an embryo and fetus. The embryonic "skeleton" is at first composed of mesenchyme shaped like bones and are the sites where ossification occurs. These "bones" provide the template for subsequent ossification, which begins during the sixth week of embryonic development and follows one of two patterns.

The two methods of bone formation, which both involve the replacement of a preexisting connective tissue with bone, do not lead to differences in the structure of mature bones, but are simply different methods of bone development. In the first type of ossification, called ***intramembranous ossification*** (in'-tra-MEM-bra-nus; *intra-* = within; *membran-* = membrane), bone forms directly within mesenchyme arranged in sheetlike layers that resemble membranes. In the second type, ***endochondral ossification*** (en'-dō-KON-dral; *endo-* = within; *-chondral* = cartilage), bone forms within hyaline cartilage that develops from mesenchyme.

Intramembranous Ossification

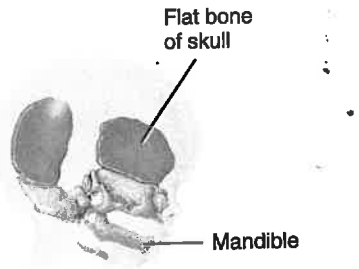
Intramembranous ossification is the simpler of the two methods of bone formation. The flat bones of the skull and mandible (lower jawbone) are formed in this way. Also, the

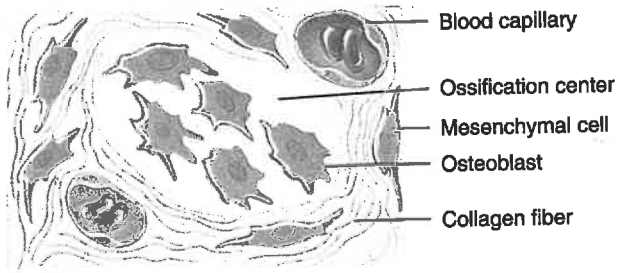
"soft spots" that help the fetal skull pass through the birth canal later harden as they undergo intramembranous ossification, which occurs as follows (Figure 6.3):

1. ***Development of the ossification center.*** At the site where bone will develop, called the ***ossification center***, cells in mesenchyme cluster together and differentiate, first into osteogenic cells and then into osteoblasts. Osteoblasts secrete the organic extracellular matrix of bone.
2. ***Calcification.*** Next, the secretion of extracellular matrix stops and the cells, now called osteocytes, lie in lacunae and extend their narrow cytoplasmic processes into canaliculi that radiate in all directions. Within a few days, calcium and other mineral salts are deposited and the extracellular matrix hardens or calcifies (calcification).
3. ***Formation of trabeculae.*** As the bone extracellular matrix forms, it develops into trabeculae that fuse with one another to form spongy bone. Blood vessels grow into the spaces between the trabeculae. Connective tissue that is associated with the blood vessels in the trabeculae differentiates into red bone marrow.

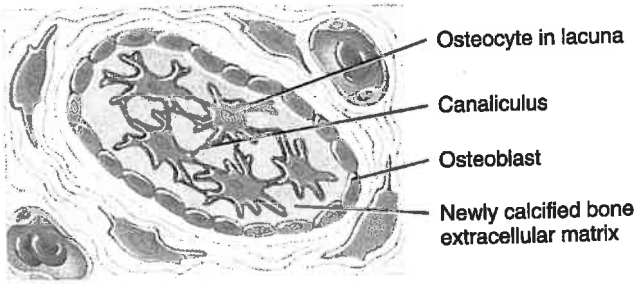
Figure 6.3 Intramembranous ossification. Illustrations 1 and 2 show a smaller field of vision at higher magnification than illustrations 3 and 4.

Intramembranous ossification involves the formation of bone within mesenchyme arranged in sheetlike layers that resemble membranes.

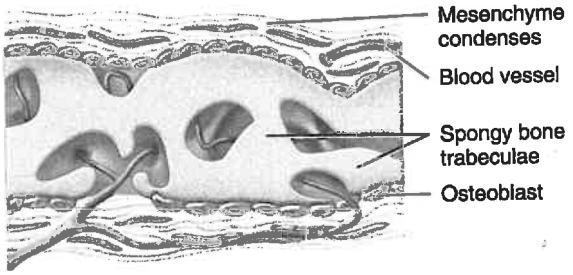




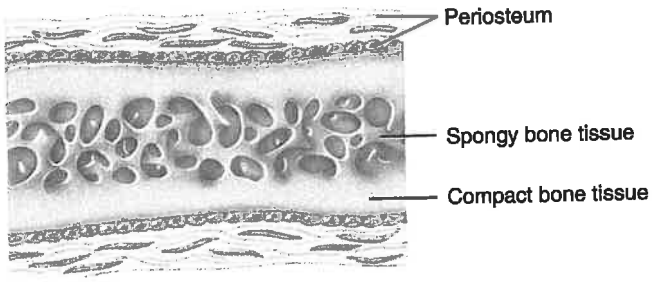
1 Development of ossification center



2 Calcification



3 Formation of trabeculae



4 Development of the periosteum

Which bones of the body develop by intramembranous ossification?

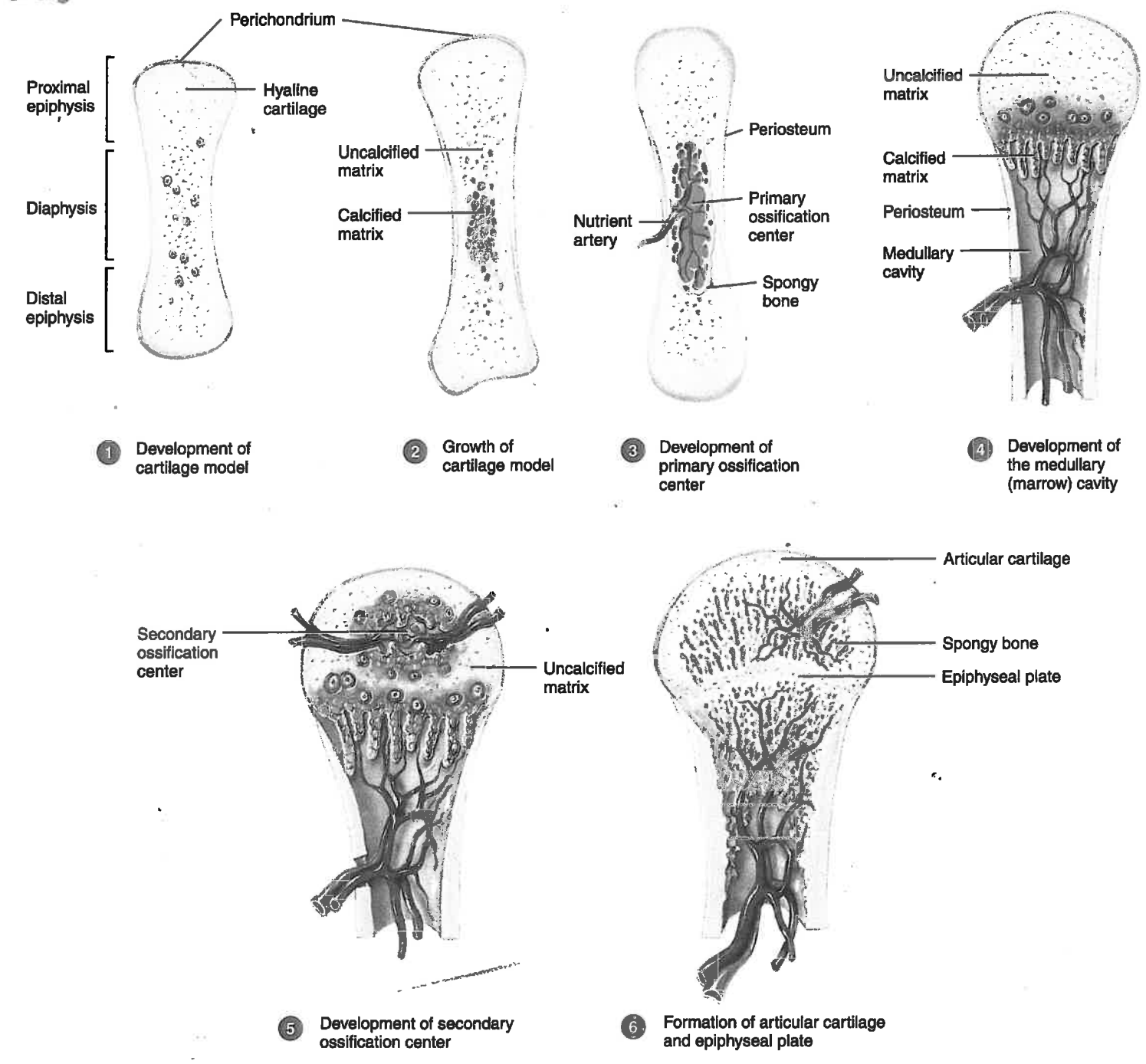
4 ***Development of the periosteum.*** At the periphery of the bone, the mesenchyme condenses and develops into the periosteum. Eventually, a thin layer of compact bone replaces the surface layers of the spongy bone, but spongy bone remains in the center.

Endochondral Ossification

The replacement of cartilage by bone is called ***endochondral ossification***. Most bones of the body are formed in this way, but as shown in Figure 6.4, this type of ossification is best observed in a long bone:

Figure 6.4 Endochondral ossification of the tibia (shin bone).

During endochondral ossification, bone gradually replaces a cartilage model.



Which structure signals that bone growth in length has stopped?

1. **Development of the cartilage model.** At the site where the bone is going to form, cells in mesenchyme crowd together in the shape of the future bone and then develop into chondroblasts. The chondroblasts secrete cartilage extracellular matrix, producing a ***cartilage model*** consisting of hyaline cartilage. A membrane called the ***perichondrium*** (per'-i-KON-drē-um) develops around the cartilage model.
2. **Growth of the cartilage model.** Once chondroblasts become deeply buried in cartilage extracellular matrix, they are called chondrocytes. As the cartilage model continues to grow, chondrocytes in its mid-region increase in size and the surrounding extracellular matrix begins to calcify. Other chondrocytes within the calcifying cartilage die because nutrients can no longer diffuse quickly enough through the extracellular matrix. As chondrocytes die, lacunae form and eventually merge into small cavities.
3. **Development of the primary ossification center.** Primary ossification proceeds *inward* from the external surface of the bone. A nutrient artery penetrates the perichondrium and the calcifying cartilage model in the mid-region of the cartilage model, stimulating osteogenic cells in the perichondrium to differentiate into osteoblasts. Once the perichondrium starts to form bone, it is known as the ***periosteum***. Near the middle of the model, blood vessels grow into the disintegrating calcified cartilage and induce growth of a ***primary ossification center***, a region where bone tissue will replace most of the cartilage. Osteoblasts then begin to deposit bone extracellular matrix over the remnants of calcified cartilage, forming spongy bone trabeculae.
4. As the primary ossification center grows toward the ends of the bone, osteoclasts break down some of the newly formed spongy bone trabeculae. This activity leaves a cavity, the medullary (marrow) cavity, in the diaphysis (shaft). The medullary cavity then fills with red bone marrow. Most of the wall of the diaphysis is replaced by compact bone.
5. **Development of the secondary ossification centers.** When blood vessels enter the epiphyses, ***secondary ossification centers*** develop, usually around the time of birth. Bone formation is similar to that in primary ossification centers except that spongy bone remains in the interior of the epiphyses (no medullary cavities are formed there). Secondary ossification proceeds *outward* from the center of the epiphysis toward the outer surface of the bone.
6. **Formation of articular cartilage and the epiphyseal plate.** The hyaline cartilage that covers the epiphyses becomes the ***articular cartilage***. Prior to adulthood, hyaline cartilage remains between the diaphysis and epiphysis as the ***epiphyseal plate***, which is responsible for the lengthwise growth of long bones.

Bone Growth in Length and Thickness

During infancy, childood, and adolescence, long bones grow in length and thickness.

Growth in Length

Bone growth in length is related to the activity of the epiphyseal plate. Within the epiphyseal plate is a group of young chondrocytes that are constantly dividing. As a bone grows in length, new chondrocytes are formed on the epiphyseal side of the plate, while old chondrocytes on the diaphyseal side of the plate are replaced by bone. In this way the thickness of the epiphyseal plate remains relatively constant, but the bone on the diaphyseal side increases in length. When adolescence comes to an end, the formation of new cells and extracellular matrix decreases and eventually stops between ages 18 and 25. At this point, bone replaces all the cartilage, leaving a bony structure called the ***epiphyseal line***. With the appearance of the epiphyseal line, bone growth in length stops. If a bone fracture damages the epiphyseal plate, the fractured bone may be shorter than normal once adult stature is reached. This is because damage to cartilage, which is avascular, accelerates closure of the epiphyseal plate, thus inhibiting lengthwise growth of the bone.

Growth in Thickness

As long bones lengthen, they also grow in thickness (width). At the bone surface, cells in the perichondrium differentiate into osteoblasts, which secrete bone extracellular matrix. Then the osteoblasts develop into osteocytes, lamellae are added to the surface of the bone, and new osteons of compact bone tissue are formed. At the same time, osteoclasts in the endosteum destroy the bone tissue lining the medullary cavity. Bone destruction on the inside of the bone by osteoclasts occurs at a slower rate than bone formation on the outside of the bone. Thus, the medullary cavity enlarges as the bone increases in thickness.

Bone Remodeling

Like skin, bone forms before birth but continually renews itself thereafter. ***Bone remodeling*** is the ongoing replacement of old bone tissue by new bone tissue. It involves ***bone resorption***, the removal of minerals and collagen fibers from bone by osteoclasts, and ***bone deposition***, the addition of minerals and collagen fibers to bone by osteoblasts. Thus, bone resorption results in the destruction of bone extracellular matrix, while bone deposition results in the formation of bone extracellular matrix. Remodeling takes place at different rates in different regions of the body. Even after bones have reached their adult shapes and sizes, old bone is continually destroyed and new bone is formed in its place. Remodeling also removes injured bone, replacing it with new bone tissue. Remodeling may be triggered by factors such as exercise, sedentary lifestyle, and changes in diet.

Orthodontics (or-thō-DON-tiks) is the branch of dentistry concerned with the prevention and correction of poorly aligned teeth. The movement of teeth by braces places a stress on the bone that forms the sockets that anchor the teeth. In response to this artificial stress, osteoclasts and osteblasts remodel the sockets so that the teeth align properly.

A delicate balance exists between the actions of osteoclasts and osteoblasts. Should too much new tissue be formed, the bones become abnormally thick and heavy. If too much mineral material is deposited in the bone, the surplus may form thick bumps, called *spurs*, on the bone that interfere with movement at joints. Excessive loss of calcium or tissue weakens the bones, and they may break, as occurs in osteoporosis, or they may become too flexible, as in rickets and osteomalacia. (For more on these disorders, see the Disorders section at the end of the chapter.) Abnormal acceleration of the remodeling process results in a condition called Paget's disease, in which the newly formed bone, especially that of the pelvis, limbs, lower vertebrae, and skull, becomes hard and brittle and fractures easily.

Fractures

A ***fracture*** is any break in a bone. Types of fractures include the following:

1. **Partial:** an incomplete break across the bone, such as a crack.
2. **Complete:** a complete break across the bone; that is, the bone is broken into two or more pieces.
3. **Closed (simple):** the fractured bone does not break through the skin.
4. **Open (compound):** the broken ends of the bone protrude through the skin.

Repair of a fracture involves several steps. First, phagocytes begin to remove any dead bone tissue. Then, chondroblasts form fibrocartilage at the fracture site and this bridges the broken ends of the bone. Next, the fibrocartilage is converted to spongy bone tissue by osteoblasts. Finally, bone remodeling occurs, in which dead portions of bone are absorbed by osteoclasts and spongy bone is converted to compact bone.

Although bone has a generous blood supply, healing sometimes takes months. The calcium and phosphorus needed to strengthen and harden new bone are deposited only gradually, and bone cells generally grow and reproduce slowly. The temporary disruption in their blood supply also helps explain the slowness of healing of severely fractured bones.

Factors Affecting Bone Growth

Bone growth in the young, bone remodeling in the adult, and the repair of fractured bone depend on several factors. These include (1) adequate minerals, most importantly calcium, phosphorus, and magnesium; (2) vitamins A, C, and D; (3) several hormones; and (4) weight-bearing exercise (exercise that places stress on bones). Before puberty, the main hormones that stimulate bone growth are human growth hormone (hGH), which is produced by the anterior lobe of the pituitary gland, and insulinlike growth factors (IGFs), which are produced locally by bone and also by the liver in response to hGH stimulation. Oversecretion of hGH produces gigantism, in which a person becomes much taller and heavier than normal, and undersecretion of hGH produces dwarfism (short stature). Thyroid hormones, from the thyroid gland, and insulin, from the pancreas, also stimulate normal bone growth. At puberty, estrogens (sex hormones produced by the ovaries) and androgens (sex hormones produced by the testes in males and the adrenal glands in both sexes) start to be released in larger quantities. These hormones are responsible for the sudden growth spurt that occurs during the teenage years. Estrogens also promote changes in the skeleton that are typical of females, for example, widening of the pelvis.

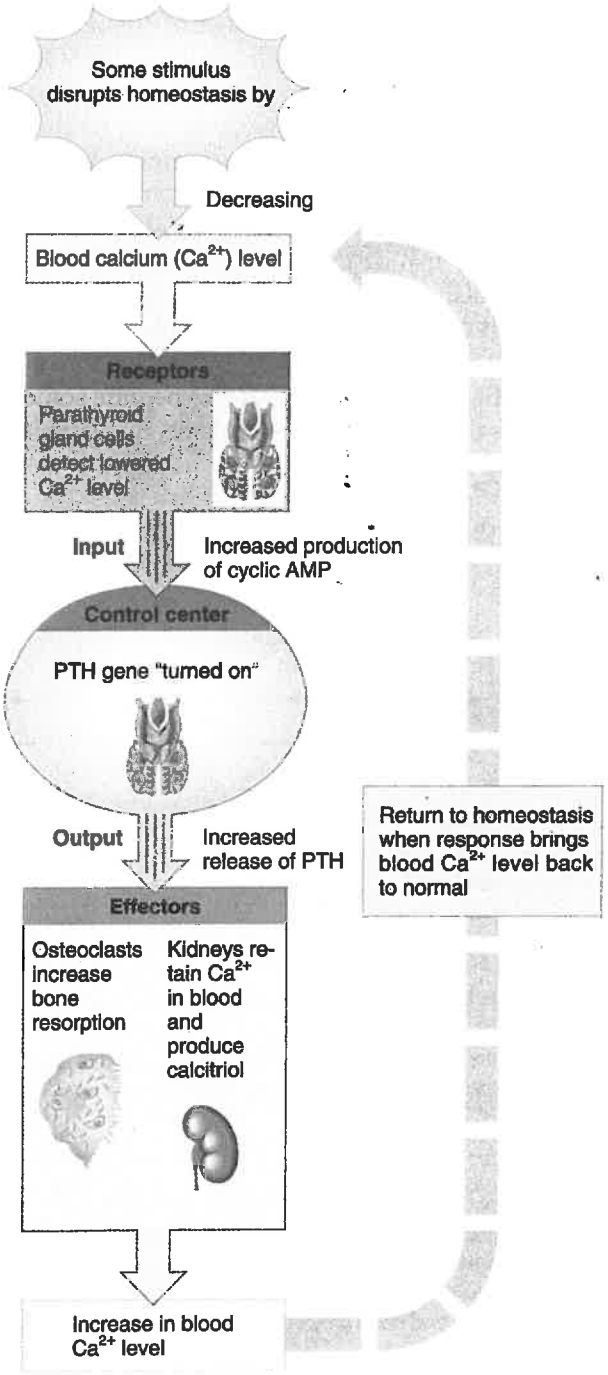
Bone's Role in Calcium Homeostasis

Bone is the major reservoir of calcium, storing 99% of the total amount of calcium present in the body. Calcium (Ca^{2+}) becomes available to other tissues when bone is broken down during remodeling. However, even small changes in blood calcium levels can be deadly—the heart may stop (cardiac arrest) if the level is too high or breathing may cease (respiratory arrest) if the level is too low. In addition, most functions of nerve cells depend on just the right level of Ca^{2+}, many enzymes require Ca^{2+} as a cofactor, and blood clotting requires Ca^{2+}. The role of bone in calcium homeostasis is to "buffer" the blood calcium level, releasing Ca^{2+} to the blood when the blood calcium level falls (using osteoclasts) and depositing Ca^{2+} back in bone when the blood level rises (using osteoblasts).

The most important hormone that regulates Ca^{2+} exchange between bone and blood is ***parathyroid hormone (PTH)***, secreted by the parathyroid glands (see Figure 13.10 on page 327). PTH secretion operates via a negative feedback system (Figure 6.5). If some stimulus causes blood Ca^{2+} level to decrease, parathyroid gland cells (receptors) detect this change and increase their production of a molecule known as cyclic adenosine monophosphate (cyclic AMP). The gene for PTH within the nucleus of a parathyroid gland cell, which acts as the control center, detects the increased production of cyclic AMP (the input). As a result, PTH synthesis speeds up, and more PTH (the output) is released into

Figure 6.5 Negative feedback system for the regulation of blood calcium (Ca^{2+}) level.

Release of calcium from bone extracellular matrix and retention of calcium by the kidneys are the two main ways that blood calcium level can be increased.



What body functions depend on proper levels of Ca^{2+}?

the blood. The presence of higher levels of PTH increases the number and activity of osteoclasts (effectors), which step up the pace of bone resorption. The resulting release of Ca^{2+} from bone into blood returns the blood Ca^{2+} level to normal.

PTH also decreases loss of Ca^{2+} in the urine, so more is retained in the blood, and it stimulates formation of calcitriol, a hormone that promotes absorption of calcium from the gastrointestinal tract. Both of these effects also help elevate the blood Ca^{2+} level.

As you will learn in Chapter 13, another hormone involved in calcium homeostasis is *calcitonin (CT)*. This hormone is produced by the thyroid gland and decreases blood Ca^{2+} level by inhibiting the action of osteoclasts, thus decreasing bone resorption.

■ CHECKPOINT

7. Distinguish between intramembranous and endochondral ossification.
8. Explain how bones grow in length and thickness.
9. What is bone remodeling? Why is it important?
10. Define a fracture and explain how fracture repair occurs.
11. What factors affect bone growth?
12. What are some of the important functions of calcium in the body?

EXERCISE AND BONE TISSUE

OBJECTIVE • Describe how exercise and mechanical stress affect bone tissue.

Within limits, bone tissue has the ability to alter its strength in response to mechanical stress. When placed under stress, bone tissue becomes stronger through increased deposition of mineral salts and production of collagen fibers. Without mechanical stress, bone does not remodel normally because resorption outpaces bone formation. The absence of mechanical stress weakens bone through decreased numbers of collagen fibers and ***demineralization***, loss of bone minerals.

The main mechanical stresses on bone are those that result from the pull of skeletal muscles and the pull of gravity. If a person is bedridden or has a fractured bone in a cast, the strength of the unstressed bones diminishes. Astronauts subjected to the weightlessness of space also lose bone mass. In both cases, the bone loss can be dramatic, as much as 1% per week. Bones of athletes, which are repetitively and highly stressed, become notably thicker than those of nonathletes. Weight-bearing activities, such as walking or moderate weightlifting, help build and retain bone mass. Adolescents and young adults should engage in regular weight-bearing exercise prior to the closure of the epiphyseal plates to help build total mass before its inevitable reduction with aging.

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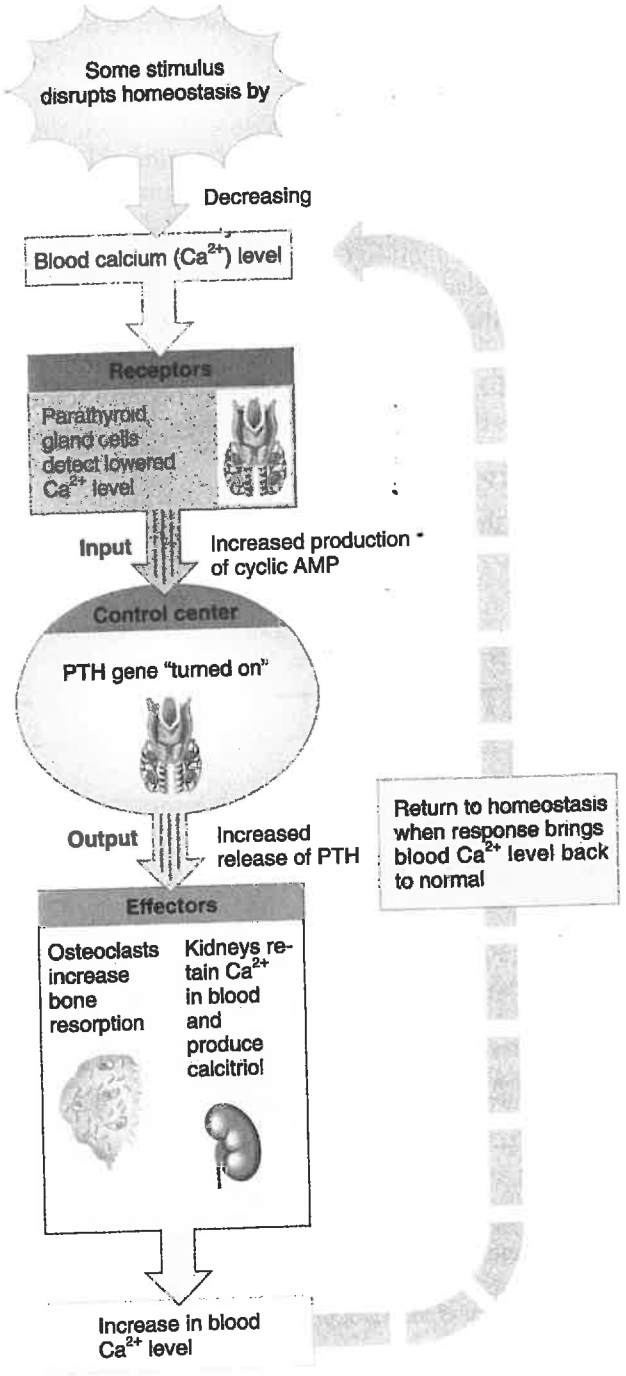

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However, the benefits of exercise do not end in young adulthood. Even elderly people can strengthen their bones by engaging in weight-bearing exercise.

Table 6.1 summarizes the factors that influence bone metabolism: growth, remodeling, and repair of fractured bones.

■ **CHECKPOINT**

13. What types of mechanical stress may be used to strengthen bone tissue?

DIVISIONS OF THE SKELETAL SYSTEM

OBJECTIVE • Group the bones of the body into axial and appendicular divisions.

Because the skeletal system forms the framework of the body, a familiarity with the names, shapes, and positions of individual bones will help you locate other organs. For example, the radial artery, the site where the pulse is usually taken, is named for its closeness to the radius, the lateral bone of the forearm. The ulnar nerve is named for its closeness to the ulna, the medial bone of the forearm. The frontal lobe of the brain lies deep to the frontal (forehead) bone. The tibialis anterior muscle lies along the anterior surface of the tibia (shin bone).

The adult human skeleton consists of 206 bones grouped in two principal divisions: 80 in the ***axial skeleton*** and 126 in the ***appendicular skeleton*** (Table 6.2 and Figure 6.6). The axial skeleton consists of the bones that lie around the longitudinal *axis* of the human body, an imaginary line that runs through the body's center of gravity from the head to the space between the feet: the bones of the skull, auditory ossicles (ear bones), hyoid bone, ribs, sternum, and vertebrae. The appendicular skeleton contains the bones of the upper and lower limbs plus the bone groups called *girdles* that connect the limbs to the axial skeleton. The skeletons of infants and children have more than 206 bones because some of their bones, such as the hip bones and vertebrae, fuse later in life.

■ **CHECKPOINT**

14. How are the limbs connected to the axial skeleton?

Table 6.1 Summary of Factors That Influence Bone Metabolism

Factor	Comment
Minerals	
Calcium and phosphorus	Make bone extracellular matrix hard.
Magnesium	Needed for normal activity of osteoblasts.
Vitamins	
Vitamin A	Needed for the activity of osteoblasts during remodeling of bone; deficiency stunts bone growth; toxic in high doses.
Vitamin C	Helps maintain bone extracellular matrix; deficiency leads to decreased collagen production, which slows down bone growth and delays repair of broken bones.
Vitamin D	Active form (calcitriol) is formed in the skin and kidneys; helps build bone by increasing absorption of calcium from small intestine into blood; deficiency causes faulty calcification and slows down bone growth; may reduce the risk of osteoporosis but is toxic if taken in high doses.
Hormones	
Human growth hormone (hGH)	Secreted by the anterior lobe of the pituitary gland; promotes general growth of all body tissues, including bone, mainly by stimulating production of insulinlike growth factors.
Insulinlike growth factors (IGFs)	Secreted by the liver, bones, and other tissues upon stimulation by human growth hormone; stimulate the uptake of amino acids and synthesis of proteins; promote tissue repair and bone growth.
Insulin	Secreted by the pancreas; promotes normal bone growth.
Thyroid hormones (thyroxine and triiodothyronine)	Secreted by thyroid gland; promote normal bone growth.
Parathyroid hormone (PTH)	Secreted by the parathyroid glands; promotes bone resorption by osteoclasts; enhances recovery of Ca^{2+} from urine; promotes formation of the active form of vitamin D (calcitriol).
Calcitonin (CT)	Secreted by the thyroid gland; inhibits bone resorption by osteoclasts.
Exercise	Weight-bearing activities help build thicker, stronger bones and retard the loss of bone mass that occurs as people age.